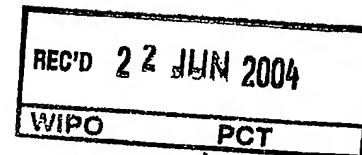




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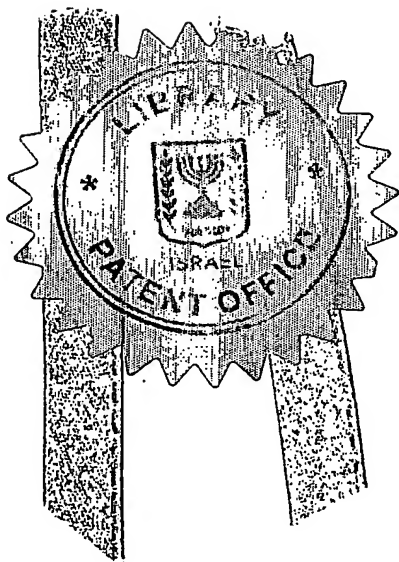
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PATENTS LAW, 5727-1967

ב ק ש ה ל פ ט נ ת  
Application for Patent

155897	מספר: Number
13-05-2003	תאריך: Date
	הוקדם/נדחה Ante/Post-dated

אני, (שם המבקש, מענו - ולגבי גוף מאוגד - מקום התאגדותו)  
I (Name and address of applicant, and, in case of a body corporate, place of incorporation)

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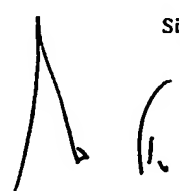
(בעברית)  
(Hebrew)

AN INDICATOR FOR MULTIWELL PLATE  
AND METHOD FOR USING THE SAME

(באנגלית)  
(English)

hereby apply for a patent to be granted to me in respect thereof.

מבקש בזאת כי ינתן לי עליה פטנט.

* בקשת חלוקה - Application for Division		* בקשת פטנט מוסף Application for Patent of Addition		* דרישת דין קדימה Priority Claim		
* מבקשת פטנט from Application		* לבקשה / לפטנט To Patent/Appl.		מספר/סימן Number/Mark	תאריך Date	מדינת האיגוד Convention Country
No. _____ מס' _____ Dated _____ מיום _____		No. _____ מס' _____ Dated _____ מיום _____				
* יפוי כח: כללי/מיוחד - רצוף בזה / עוד יוגש P.O.A.: general / specific - attached / to be filed later - הוגש בעניין _____ Has been filed in case _____						
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\* מחק את המיותר Delete whatever is inapplicable

סמן לפלטה מרובת-בארות ושיטה לשימוש בו

AN INDICATOR FOR MULTIWELL PLATE  
AND METHOD FOR USING THE SAME

ממציא: עמוס ולינסקי

## FIELD OF THE INVENTION

The present invention generally relates to an indicator for multiwell plate, more specifically, to a pierceable foil covering the upper portion of the multiwell plate so the pipette tip is directed to either puncture or perforate said foil while delivering the sample into each of the wells, thus indicating the well was filled with said sample. The present invention also relates to a method for using the indicator in every day laboratory practice and for a method for producing the same.

## BACKGROUND OF THE INVENTION

Multi-well plates are widely used in the every day laboratory practice for simultaneous processing of discrete quantities of flowable material, especially for the purpose of e.g. purification, concentration or extraction of target substances. The plates usually comprises a body with a plurality of receptacles each having an entry end opening for introduction of an individual charge of the flowable material and an exit opening for outflow of at least part of the material. Most of the commercially available multi-well plates are laid out with 96 wells in an 8 x 12 array (mutually perpendicular 8 and 12 well rows). The dimensions of the aforementioned 96-well plates are standardized. Those plates are typically used as reaction vessels in which various tests and assays are performed. Those tedious sampling techniques require high measure of concentration, for that the technician should be aware for the position of the last well sampled.

Although that those plates usually comprise various auxiliaries and attachments, suitable for the specific laboratory or processing requirements, means for positioning the last well sampled. Thus, US Pat. No. 2003,008,412 to Hong *et al.* presented plate alignment and sample transfer indicia for a multiwell multiplate stack. According to their invention, a first multiwell plate is stacked atop a second multiwell plate. The first multiwell plate has x wells arranged in an array, each well is capable of receiving a sample and has an outlet. The second multiwell plate has y wells arranged in an array, each well being capable of receiving a separate sample. Similarly, GB Pat. No. 2,377,990 to Fischer-Fruhholz *et al.*, introduced an ion exchange or a filtration membrane located on top of the upper portion of the multiwell plate. This thin

member is affixed to the body by bonding to close the exit openings of the receptacles and form an external face of the device.

It is hence a strong felt need to acquire such a disposable, cost effective indicator, useful for positioning sampled wells in commercially available multiwell plates.

## SUMMARY OF THE INVENTION

It is thus one purpose of the present invention to provide an indicator for a multiwell plate. According to a general embodiment of the present invention, said plate is consisting of a predetermined array of wells, such as a plate especially adapted for either proceeding or analyzing enzymatic reactions, or a PCR, ELISA or an FID ninety six wells sampling plate, comprising a conformation of 12x8 array of wells.

The hereto defined indicator comprising (i) a pierceable foil member adapted to cover the top portion of the plate, and (ii) an array of signs located on the upper surface of said foil member, adapted to indicate the location of the said array of the wells. The aforementioned foil is further adapted to cover the top of the plate so at least a portion of said array of signs is overlapping said array of wells. Moreover, the foil member is characterized by that it is pierced by a means of a pipette at the location of said sign, a noticeable deformation is obtained at the upper surface of said foil member, so a clear indication is provided.

The term 'multiwell plate' is referring along the present invention to any assembly comprising a plurality of about 1 $\mu$ l to about 1ml or more wells.

The term 'pipette' is referring along the present invention to any sampling device, selected, yet not limited to a pipette, tip, injector, syringe, mechanical or electronically driven calibrated pipette, and especially to those pipettes used in every day practice of the biochemical, medical or other laboratory, such as the Eppendorf pipettes, and most particularly to those pipettes adapted for a routine work and extended with a disposable plastic tip.

The term 'a pierceable foil member' is referring along the present invention to any thin leaf-like sheet, easy to be pierced, punctured, protruded, perforated or penetrated by a means of the pipette, as defined above, or by a tip member extended from said pipette.

It is according to another embodiment of the present invention, wherein the aforementioned pierceable foil member is framed by a frame adapted to fit by size and shape the perimeter of the multiwell plate. According to yet another embodiment of the present invention, the frame is made of metal substances, polymeric compositions or a combination thereof. It is acknowledged in this respect that the frame is either elastic or rigid and may comprise of various auxiliaries, such as signs (rows and column identification or numeration), attachments (such as a top-cover or an upper screen) etc. It is well in the core of the present invention, wherein the pierceable foil and the attached frame are one integrated disposable product.

It is according to another embodiment of the present invention, wherein the pierceable foil member is made of metallic substances, polymeric compositions or a combination thereof. Most preferably, said pierceable foil member is an aluminum foil. It is well acknowledged that the foil may be coated by a second layer, such as a lacquer, or alternatively comprises of a multilaminal configuration.

According to another embodiment of the present invention, the pierceable foil member is a perforated foil and hence comprises a plurality of perforation, cuts, holes or bores of any shape and size. Hence, it is in the scope of the present invention wherein the pierceable foil member is a perforated foil, comprising an array of punctures. Moreover, said array is preferably adapted to overlap at least a portion of the array of the wells. It is further acknowledged that for many purposes, the number of the perforations as defined above is equal to the number of the wells. Nevertheless, for few specific purposes, the number of the perforation is less than the number of the wells, so some of the wells remain intact, sealed and thus are not sampled.

The diameter of the punctures of the perforated foil is preferably equal or smaller than the diameter of the well's internal bore, so the piercing by the pipette shall remain a noticeable deformation. The diameter of said puncture may range in case of

commercial available multiwell plates used in the laboratory routine practice from about 1 to about 10 mm, preferably about 3 to 4 mm. Hence for example, for a well comprising an internal bore of 1 mm, a puncture having a diameter of 0.5 mm is suitable. According to another embodiment of the present invention, the pierceable foil member comprising at least one tiring line adjacent to the signs, so at the time said foil is pierced, it is tired at a predetermined measure, size or shape along said one or more tiring lines. Said tiring lines are characterized by every shape or size, such as straight-line, circular line, polygonal or star-like shape etc. The tiring lines are obtained by various technological processes, such as pressing metal sheets, LASER-based cutting processes, photochemical etching techniques etc.

The present invention also provided a novel, cost effective and very convenient multiwell plate, especially adapted to routine laboratory practice of sampling comprising the indicator as defined in any of the above.

Furthermore, the present invention provides for an accurate and easy to handle method for indicating each sampled well in a multiwell plate. Said method comprising the following steps: (i) mounting the pierceable foil member on top of the multiwell plate in the manner the array of the signs is overlapping at least a portion of the array of the wells; subsequently (ii) piercing said foil by a pipette, so the foil is deformed in a noticeable manner; and lastly (iii), sampling the well by a means of delivering the sample from the pipette to inner portion of the well or *vice versa*. This short and effective method of indications is characterized that by the deformation of the foil, each sampled well is effectively indicated. Most importantly, faulted actions of either double sampling or abstained sampling are thus completely avoided.

## BREIF DESCRIPTION OF THE INVNETION

In order to understand the invention and to see how it may be carried out in practice, a preferred embodiment will now be described, by way of non-limiting example only, with reference to the accompanying drawing, in which

figure 1 schematically presents a perspective view of a commercially available multiwell plate;

figure 2 schematically presents a perspective view of a pierceable foil member according to one embodiment of the present invention;

figure 3 schematically presents a perspective view of a frame according to another embodiment of the present invention;

figure 4 schematically presents a perspective view of a frame and a pierceable foil member according to another embodiment of the present invention;

figure 5 schematically presents figure 1 schematically presents a lateral cross-section of a commercially available multiwell plate, covered by pierceable foil member in a frame according to another embodiment of the present invention; and

figure 6 schematically presents a top view of a pierceable foil member and the signs located on its top surface according to yet another embodiment of the present invention.



## DETAILED DESCRIPTION OF THE INVENTION

The following description is provided, along all chapters of the present invention, so as to enable any person skilled in the art to make use of said invention and sets forth the best modes contemplated by the inventor of carrying out this invention. Various modifications, however, will remain apparent to those skilled in the art, since the generic principles of the present invention have been defined specifically to provide an indicator, especially useful for avoiding faulted actions of either double sampling or abstained sampling.

Reference is thus made to figure 1, presenting a schematic illustration of a multiwell plate (10), comprising a 9x3 array of wells, such as well (11). Rows and columns are usually been indicated by alphabetical (here: A to I) and numerical (here: 1-3) consequent signs.

Reference is made now to figure 2, presenting a schematic illustration of a pierceable foil member (20), comprising the hereto-defined 9x3 array of signs. Each sign is characterized here by a circular draw and an X-like indication (See for example sign 21, located in the A-3 position in the aforementioned array.

It is yet further acknowledged in this respect that according to one particularly preferred embodiment of the present invention, the indicator for a multiwell plate comprising a pierceable foil, which comprises an array of previously produced punctures, wherein said punctures are having a diameter smaller than the diameter of the bore, so while delivering the sample by a suitable pipette, the tip portion of the pipette deforms the foil (namely, increasing the diameter of the said puncture) in a noticeable manner.

Reference is made now to figure 3, presenting a schematic illustration of the frame (30), in a perspective view, which does not include the attached pierceable foil member (20). It is hence acknowledged that frame (30) is adapted to fit the top portion of plate (10) and thus to be effectively anchor foil (20) on top of plate (10) in the overlapping desired orientation

Reference is made now to figure 4, presenting a perspective schematic illustration of the frame (30), and the attached pierceable foil member (20). The pierceable foil member comprises a plurality of signs, adapted to overlap a 9x6 array of wells. Intact sign (see 41 for example) is characterized by a circular draw and a central X-like indication. The tip portion of a pipette (42) is piercing sign (43), which corresponds to well number A-6 (not shown), and deformed the foil irreversibly, to obtain a star-like tiring pattern on the foil.

Reference is made now to figure 5, presenting a schematic lateral cross-section illustration of the plate (10), the pierceable foil member (dark line, 20) and the frame (30). Plate (10) comprises of 9 wells in a row, such as indicated well (11). The tip portion of the pipette (42) is piercing the foil member (20) in the manner the tip is located inside the inner portion of the well. While penetrating throughout the foil (20), a irreversible and noticeable deformation is obtained in the area (43) located adjacent to the tip (42).

Reference is made now to figure 6, presenting a schematic top view of various embodiments of the pierceable foil member (20). Hence, a circular drawn line is presented in view 6A, and a doubled line structure is presented in view 6B. A X-like pattern is described in view 6C.

A circular drawn pattern is provided in view 6D. This pattern is accompanied with a plurality of tiring lines (64), located inside the perimeter of the drawn circle. View 6E shows the same, wherein the tiring line is exceeded outside the respectively small and central drawn line.

A round preformatted puncture (66) is presented in view 6F. According to this preferred embodiment of the present invention, the piercing of the foil (20) is respectively easy and fast, whereat and fine enlargement of the newly made hole's diameter is well obtained. Similarly, a polygonal shape (here, squared pattern) preformatted puncture is presented in view 6G.

It is well in the scope of the present invention wherein a combination of those embodiments is provided. Thus for example, a round preformatted puncture (66) is

provided together with a plurality of tiring lines (67) as presented in view 6F. Other embodiments, such as combination of drawing patterns, preformatted punctures and tiring lines are also possible.

## CLAIMS

1. An indicator for a multiwell plate consisting a predetermined array of wells, said indicator comprising
  - a. a pierceable foil member adapted to cover the top portion of the plate;
  - b. an array of signs located on the upper surface of said foil member, adapted to indicate the location of the said array of the wells;wherein said foil is adapted to cover said plate so at least a portion of said array of signs is overlapping said array of wells, so when the foil member is pierced by a means of a pipette at the location of said sign, a noticeable deformation is obtained at the upper surface of said foil member and a clear indication is provided.
2. The indicator according to claim 1, wherein the pierceable foil member is framed by a frame adapted to fit by size and shape the perimeter of the multiwell plate.
3. The indicator according to claim 2, wherein the frame is made of metal substances, polymeric compositions or a combination thereof.
4. The indicator according to claim 2, wherein the frame is either elastic or rigid.
5. The indicator according to claim 1, wherein the pierceable foil member is made of metallic substances, polymeric compositions or a combination thereof.
6. The indicator according to claim 5, wherein the pierceable foil member is an aluminum foil.
7. The indicator according to claim 1, wherein the pierceable foil member is a perforated foil.
8. The indicator according to claim 7, wherein the pierceable foil member is a perforated foil, comprising an array of punctures; said array is adapted to overlap at least a portion of the array of the wells.
9. The indicator according to claim 8, wherein the diameter of the punctures of the perforated foil is smaller than the diameter of the well's internal bore.

10. The indicator according to claim 1, wherein the pierceable foil member comprising at least one tiring line adjacent to the signs, so at the time said foil is pierced, it is tired at a predetermined measure, size or shape along said one or more tiring lines.
11. The indicator according to claim 1 or any of its preceding claims, as described in figure 2.
12. The indicator according to claim 2 or any of its preceding claims, as described in figure 4.
13. The indicator according to claim 1 or any of its preceding claims, comprising one or more of the signs described in figure 6.
14. A multiwell plate comprising the indicator as defined in claim 1 or in any of its preceding claims.
15. A method for indicating each sampled well in a multiwell plate comprising;
- a. mounting the pierceable foil member on top of the multiwell plate in the manner the array of the signs is overlapping at least a portion of the array of the wells;
  - b. piercing said foil by a pipette, so the foil is deformed in a noticeable manner; and
  - c. sampling the well by a means of delivering the sample from the pipette to inner portion of the well or *vice versa*;
- characterized that by said deformation of the foil, each sampled well is effectively indicated and faulted actions of either double sampling or abstained sampling are avoided.



Dr Eyal Bressler, Patent Attoreny  
T (972)-2-5865658 F -2-5865657

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FIGURE 1

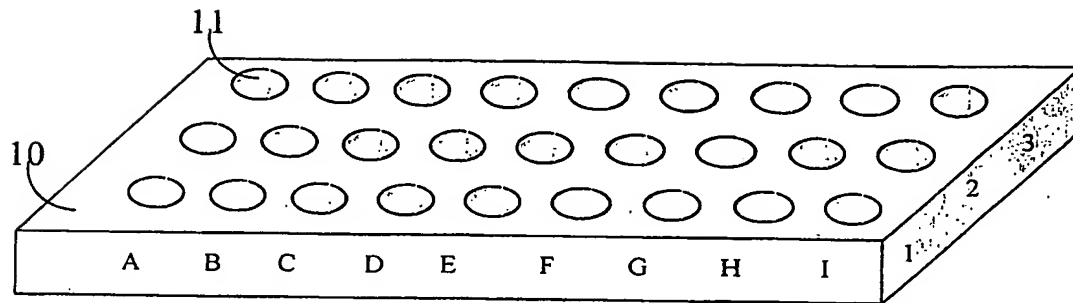


FIGURE 2

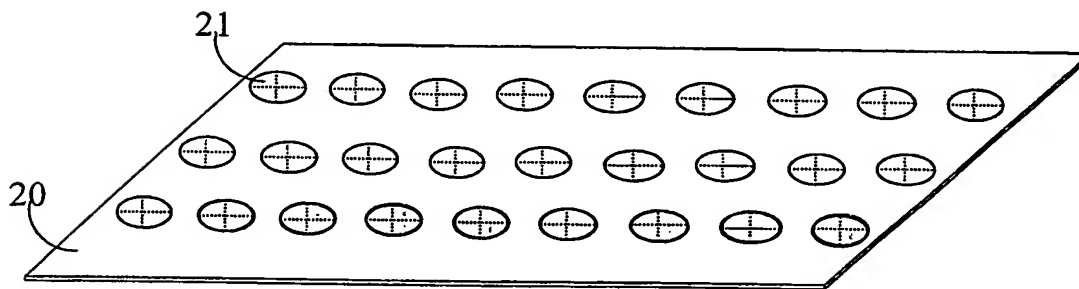


FIGURE 3

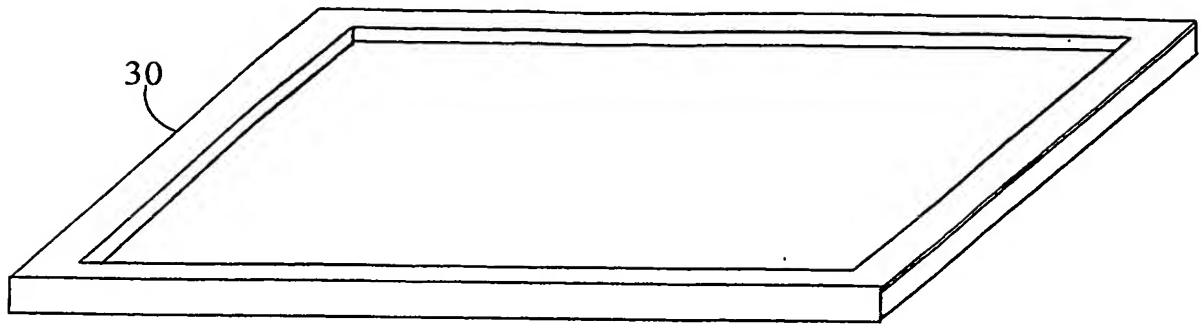


FIGURE 4

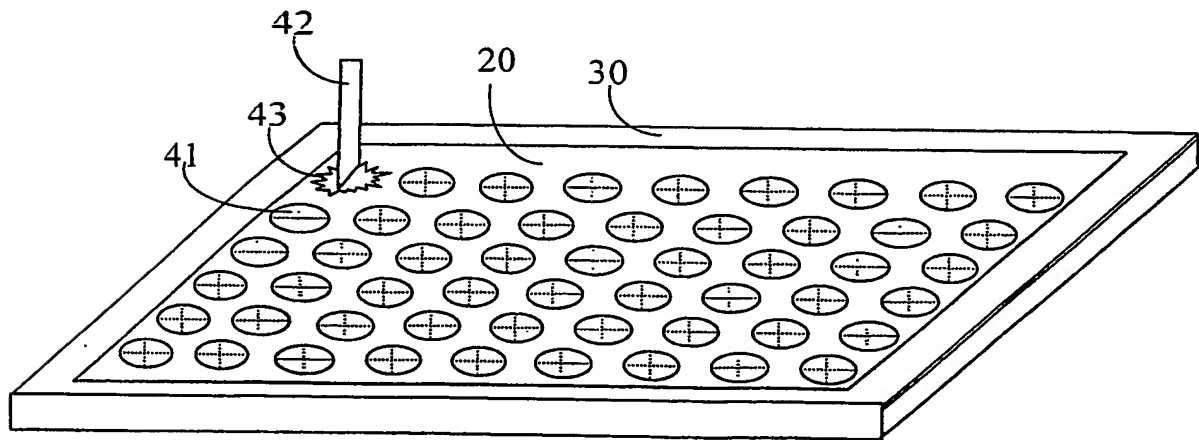


FIGURE 5

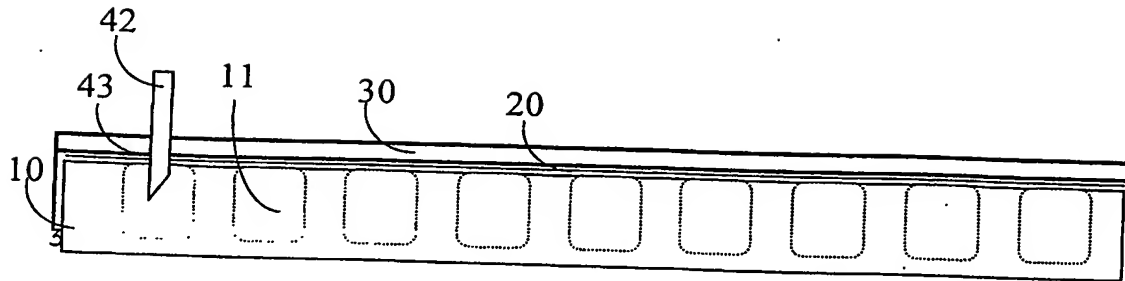


FIGURE 6

